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CROWELL & MORING LLP
INTELLECTUAL PROPERTY GROUP
P.O. BOX 14300
WASHINGTON, DC 20044-4300

EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/678,650	HAKENBECK, REGINE	
	Examiner	Art Unit	
	CYNTHIA B. WILDER	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5,6,8-11,13-17 and 21-26* is/are pending in the application.

4a) Of the above claim(s) *15-17* is/are withdrawn from consideration.

5)☒ Claim(s) *11,14 and 21* is/are allowed.

6)☒ Claim(s) *1,3,6,8-10 and 24-26* is/are rejected.

7)☒ Claim(s) *5,22 and 23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed is acknowledged and has been entered. Claims 1, 3, 5, 8-11, 14, 22 and 23 have been currently amended. Claims 2, 4, 7, 12, 13, 18-20 have been canceled. Claims 24-26 have been added. Claims 1, 3, 5, 6, 8-11, 14-17, and 21-26 are pending. Claims 15-17 are withdrawn from consideration as being drawn to a non-elected invention. Claims 1, 3, 5, 6, 8-11, 14, 21-26 are pending and discussed in this Office action. All of the arguments have been thoroughly reviewed and considered but deemed moot in view of the new grounds of rejections necessitated by applicant's amendment of the claims. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

This action is made FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Previous Rejection

3. The prior art rejection under 35 USC 103(a) directed to claims 1 and 6 as being unpatentable over Dowson et al in view of Kell is withdrawn. The prior art rejection directed to claims 2-3 as being unpatentable over Dowson et al in view of Kell and further in view of *In re Deuel* is withdrawn. The claim rejection under 35 USC 112 second paragraph directed to claims 1, 4, 6, 8-11, 14, 22 and 23 are withdrawn in view of Applicant's amendment and/or cancellation of the claims. The double patenting rejection is withdrawn in view of Applicant's submission of a proper terminal disclaimer under 37 CFR 3.73(b).

New Ground(s) of Rejections

THE NEW GROUND(S) OF REJECTIONS WERE NECESSITATED BY APPLICANT'S AMENDMENT OF THE CLAIMS:

Claim Objections

4. Claims 1 and 9 are objected to because of the following informalities:

(a) Claim 1 is objected because there appears to be typo at line 6 of step (ii). It is suggested changing "n" to --in--. Appropriate correction is required.

(a) Claim 9 is object for being grammatically incorrect for the phrase "specific for penicillin a PBP gene of sensitive strains" because penicillin is not a PBP gene. It is suggested amending the claim to recite the phrase --specific for a PBP gene of penicillin sensitive strains". Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 25 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claim 25 lacks proper antecedent basis for "the melting point of he DNA probes" because the claim 24 from which it depends does not recite any melting point temperature and thus it cannot be determined how one is to determine what temperature is required for the hybridization reaction in the claimed method.

Claim Rejections - 35 USC § 103

5. The following are new grounds of rejections necessitated by Applicant's amendments. Although the claims were previously rejected as being unpatentable over the same references, Applicant's amendments have necessitated the inclusion of new grounds of rejections in the present rejection(s). It is noted that, to the extend that they apply to the present rejection(s); Applicant's arguments are addressed following the rejection.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1, 6, 8-10, 24-26 are finally rejected under 35 U.S.C. 103(a) as being unpatentable over Dowson et al (citation made of record in prior Office action) in view of Kell et al (citation made of record in prior Office action). Regarding claims 1 and 24, Dowson et al. disclose a method for identifying penicillin-sensitive or penicillin-resistance streptococci previously not known to have antibiotic resistance comprising: isolating bacterial DNA and hybridizing the DNA with at least one sensitivity-specific DNA probe (Pn12) and at least one resistance-specific DNA probe (Pn11 and Pn13) (page 5859, right column second full paragraph) that specifically hybridizes to a DNA sequence specific to a penicillin binding protein gene (PBP2B) of penicillin sensitive strains of *Streptococcus pneumoniae* (page 5859, right column second full paragraph)

and determining whether or not the streptococci strain is sensitive to penicillin or not by detecting which probe or probes hybridize (see page 5859 and Table 1, which recite Streptococci and strains wherein antibiotic resistance has not be determined (ND)) or wherein view little to high levels of resistance or sensitivity to penicillin has been determined).

Regarding Claim 6, Dowson et al disclose the method wherein the probes are labeled radioactively (page 5859, right column, lines 4-6).

Regarding claims 8-10, Dowson et al disclose wherein the DNA obtained is hybridized to more than one DNA probe to a DNA sequence specific for a PBP gene of penicillin resistant strains of Streptococcus pneumoniae ((Pn11, Pn13) and more than one DNA probe specific to a DNA sequence specific for a PBP gene of penicillin sensitive strains of Streptococcus pneumoniae (Pn12 and fragment from the PBP2B gene of the penicillin sensitive strain R6) (page 5859, second full paragraph , column 2).

Regarding claim 25-26, Dowson et al disclose wherein the hybridization conditions were carried out by standard techniques using stringent conditions as defined by Maniatis et al (Molecular Cloning, Cold Spring Harbor Laboratory) (see lines 5-6 of col. 2 at page 5859). The specification supports the use of Maniatis as teaching the stringent hybridization conditions of the instant invention (see page 5, first full paragraph). Accordingly, Dowson meets these limitations.

Dowson et al do not expressly teach wherein the screening assay includes DNA from *S. pneumoniae* having unknown resistance to penicillin. However, Dowson provides sufficient evidence to the ordinary artisan to screen and/or test any

streptococci strain having unknown resistance to penicillin using the claimed method steps. Dowson provides sufficient motivation for performing a screening assay as claimed using probes which specifically hybridizes to sequences specific to penicillin binding protein genes. Dowson et al teach in the introduction that the emergence of resistance to penicillin in a number of bacterial species has occurred by the development of altered high molecular weight penicillin-binding proteins that have reduced affinity for the antibiotic (page 5858). Dowson et al identifies regions in two of the PBP2B genes of penicillin resistant pneumococci that have been found to be altered in all penicillin resistance pneumococci and teaches wherein probes are designed to target this region in order to determine antibiotic resistance in Streptococci bacterial strains (page 5859).

Kell et al supports the teaching of Dowson et al. Kell et al teach that "penicillin resistance in Streptococcus pneumonia (the pneumonococcus) is entirely due to the development of altered forms of penicillin-binding proteins (PBPs) that have decreased affinity for beta-lactam antibodies". Kell et al teach that "the PBP genes of penicillin resistance pneumococci have a mosaic structure, consisting of regions that are very similar to the corresponding regions in the genes from penicillin-susceptible pneumococci and regions that differ by as much as 20% in nucleotide sequences (see page 4382). Kell et al also teaches hybridization method steps and hybridization conditions using probe(s) targeted to sequences specific for PBP genes in order to fingerprint penicillin resistant pneumococci (see abstract 4383 and 4384).

Thus, it would have been obvious to one of ordinary skill in the art at the time of the claimed invention that the claimed invention of Dowson et al in view of Kell et al could be modified to screen any pneumococci sample having unknown penicillin resistance with a reasonable expectation of success. It would have obvious to a person of ordinary skill in the art to try to screen various DNA samples having no known penicillin resistance using the method of Dowson in view of Kell et al in an attempt to provide alternative means of screening for new or different strains of antibiotic resistant pneumococci for epidemiological studies as taught by both Dowson et al and Kell et al.

Response to Arguments

Applicant's Traversal

8. Applicant traverses the rejection on the following grounds: Applicant states that their method provides for the accurate determination even if a probe that is specific for the particular resistance gene of the assayed isolate is not used. Applicant states that therefore penicillin resistance can be determined by Applicant's method without the necessity of using probes that are specific for every possible S. pneumonia resistance gene. Applicant summarizes Dowson's invention and states that Dowson studies the relatedness among different species by screening the various different species for resistant-specific DNA sequences. Applicant states that a person of ordinary skill in the art would have to modify Dowson's method so that the probes specific for penicillin-resistance in S. pneumoniae and specific for penicillin sensitive S. Pneumoniae would be used to screen the same species, i.e., Spneumoniae, rather than studying the relatedness of different species; e.g., S. sanguis or S. oralis. Applicant states that such

modifications would render Dowson's method unsatisfactory for its intended purpose, which is to study the transfer of altered PBP genes for S. pneumonia into different streptococci species. Applicant states that Kell does not overcome the dfinciencies of Dowson. Applicant states that the combination of Dowson and Kell do not teach the instant invention because the combination fails to determine whether a strain is sensitive or resistant to penicillin and further does not teach or suggest discriminating between sensitive and resistant strains.

Examiner's Response

9. All of the arguments have been thoroughly reviewed and considered but are not found persuasive. In response, the Examiner acknowledges Applicant's arguments but notes that Applicant's claims as currently claimed are not commensurate in scope with the arguments made of record. The claims as currently amended are not limited in the manner argued by applicant and thus the conclusion drawn by Applicant are not apparent. The newly added limitations as recited in the claim 1 and new claim 24 do not define the structure of the DNA sequence of the PBP gene to which the claimed DNA probe(s) are to hybridize and likewise they do not define the structure of the claimed DNA probe which is intended to be specific for the undefined DNA sequence of the PBP genes. No structural features of the claimed probes or DNA sequence of the PBP gene is given. Thus the claims encompass the teachings of Dowson et al Dowson et al identifies regions in two of the PBP2B genes of penicillin resistant pneumococci that have been found to be altered in all penicillin resistance pneumococci and teaches wherein probes are designed to target this region in order to determine antibiotic

resistance in Streptococci bacterial strains (page 5859). The examiner maintains that the combination of Dowson et al in view of Kell meets the limitations of the claims as Kell supports the teachings of Dowson and further teaches hybridization method steps using probe(s) targeted to sequences specific for PBP genes in order to fingerprint penicillin resistant pneumococci (see abstract 4383 and 4384). The combination of Dowson in view of Kell clearly suggest that it is within the ordinary artisan technical grasp to screen a variety of sample for Streptococcus pneumoniae sensitivity or resistance using specific probes which target the PBP gene of penicillin resistance pneumococci when the sequences of the PBP gene are different. Applicant provides no sufficient evidence to support the conclusions that the Dowson in view of Kell does not teach the instant invention. Accordingly, the rejection is maintained.

Claim Rejections - 35 USC § 103

10. Claim 3 is finally rejected under 35 U.S.C. 103(a) as being unpatentable over Dowson et al (citation made of record in prior Office action) in view of Kell et al (citation made of record in prior Office action) and further in view of *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995).

Regarding 3, Dowson et al. teach a method for identifying penicillin resistance in bacteria comprising: isolating bacterial DNA and hybridizing the DNA with at least one sensitivity-specific and at least one resistance-specific probe (page 5859, right column, and second full paragraph). Additionally, they teach that the PBP genes in penicillin sensitive and resistant strains of *S. pneumoniae* comprise highly conserved regions

alternating with highly divergent regions (Abstract). Dowson et al. do not teach the sensitivity-specific probes are selected from SEQ ID NO: 7-13.

Kell et al. teach the PBP2x gene sequence of penicillin-resistant pneumococci and sequences which confer antibiotic resistance to pneumococci in patients wherein said sequence comprises the sequence of SEQ ID NO: 8 (see accession number z21803 and Figure 4). Kell et al distinguishes between sequences of pneumococci that resistant and susceptible to penicillin (see page 4388).

In the court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed sequence of the instant invention simply represent a structural homolog of the nucleotide sequences taught by Kell et al derived from sequences expressly suggested by the prior art of and known in the prior art as derived from PBP2x gene of penicillin-resistant pneumococci and useful for detecting penicillin resistance in Streptococci strains, and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed

nucleotide sequences are *prima facie* obvious over the cited references in the absence of secondary considerations.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the PBP2x gene sequence differences between antibiotic sensitive and antibiotic resistant strains and to use probes which hybridize to those sequences in the method of Dowson et al. for identifying antibiotic resistant bacteria for the obvious benefit of identifying clinically important antibiotic-resistant bacteria efficiently and economically using DNA hybridization and antibiotic response-specific probes.

Response to Arguments

Applicant's traversal

11. Applicant traverses the rejections above on the following grounds: Applicant states that Dowson et al in view of Kell et al do not provide any incentive for one of skill in the art to make probes that can hybridize to various gene types of resistance, because such probes would not be specific for a particular class of resistance gene. Applicant states that the Kell teaches a sequence SEQ ID NO: 8 (noted by the Examiner) that is a sequence of the penicillin susceptible strain R6. Applicant states that a skilled person would not have been motivated to modify Dowson to use a sensitivity-specific DNA sequence consisting of SEQ ID NO: 8 in combination with a resistant specific DNA sequence of S. pneumonia to test a Streptococcus pneumoniae of unknown resistance for resistance to penicillin because such a modification would

have rendered the method of Dowson unsatisfactory for Dowson's intended purpose as discussed above.

Examiner's Response

12. All of the arguments have been thoroughly reviewed and considered but not found persuasive for the reasons that follow: In response to Applicant's arguments concerning the combination of Dowson et al in view of Kell, the Examiner notes again that Applicant's arguments are not commensurate in scope with the claims as currently written. Applicant is reminded that the claims do not define the DNA sequence of the of the PBP gene the claimed probes are intended to be specific for. The sequence of the DNA probe recited in the claim 3 comprises a structure substantially identical to the sequence as taught by Kell (see claims and alignment below):

```
SEQ ID NO: 8          1 AACAGTTCTGCTGAAGAAG 19
                        ||||||||||||||||||
Kell                314 AACAGTTCTGCTGAAGAAG 332.
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Kell expressly teaches that the sequence is part of the PBP 2X gene of penicillin resistant pneumococci (See Figures and attachment to reference mailed 3/20/2007). Kell further teaches isolating oligonucleotide sequences for use in PCR assays to fingerprint penicillin resistance strains of Streptococcus pneumoniae. Accordingly, the arguments are not found persuasive.

Conclusion

13. Claims 1, 3, 6, 8-10, 24-26 have been rejected. Claims 5 and 22-23 are objected because they depend from rejected claims. Claims 11, 14 and 21 contain allowable subject matter.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CYNTHIA B. WILDER whose telephone number is (571)272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/GARY BENZION/
Supervisory Patent Examiner, Art Unit 1637